

FACILITY FORM 602

MODERN STATE AND PROSPECTS FOR THE SOLUTION
OF THE PROBLEM OF THE ORIGIN OF LIFE

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ABSTRACT. The appearance of life on earth was the final event of millions of years of "prebiological" evolution taking place under radiational and chemical conditions no longer existing on the planet. The initial stage of this evolution was the appearance of hydrocarbons, now known to arise spontaneously both on earth and elsewhere in the universe; from these were formed multimolecular compounds, and ultimately more extensive systems capable of self-renewal. The structure and behavior of these early systems can be simulated by physico-chemical objects such as coacervate drops, which react with their environment as open systems, and which exhibit "protometabolic" activity based on the absorption of catalytic substances. Initial studies made with such models suggest that ultimately the synthesis of protoplasm may become possible with the use of similar techniques.

The present situation as regards the problem of the origin of life is characterized by the radical turnabout regarding this issue which took place among natural scientists under our eyes at the middle of the twentieth century. /656¹

Whereas in 1932, F. Hopkins (Hopkins, 1933) in his presidential address before the London Royal Society emphasized the complete lack of information among scientists regarding this "most improbable event in the history of the universe", only three decades later G. Quinby (Quinby, 1966) in opening a Florida conference on prebiological systems, stated with complete justification that "the question of the origin of life exercises an evident and indefinable fascination for all mankind," and that "the problem is now ready for an attack by the powers of intellectual artillery."

Actually, during recent years a number of countries have been holding numerous conferences and symposiums on this particular problem, which is also dealt with in a great many scientific papers. In a number of countries (the United States and Japan, for instance) educational programs, textbooks and manuals on biology begin with a presentation of the problem of the origin of life. The subject figures in numerous monographs, summaries and chrestomathies.

Research carried out by Soviet scientists played a decisive role in the

¹Numbers in the margin indicate pagination in the foreign text.

turnabout referred to. The earlier, widely practiced mechanical approach to understanding the essence of life failed to reveal any rational routes for studying the origin of this phenomenon. On this basis the rise of life on earth appeared to be a great rarity, a "happy accident" that couldn't occur again, an event beyond the grasp of objective scientific study, something in the realm of faith rather than knowledge.

By contrast, very large circles of scientists around the world, under the influence of ideas developed by Soviet researchers on the basis of the dialectic materialistic view of life, now acknowledge that the rise of life on earth was a "regular" event, in fact an inevitable and integral part of the general development of the universe, and hence something entirely accessible to scientific study. It is an important fact that in connection with this concrete methods have been discovered for the scientific solution of this problem which interests us—both on the basis of objective observations made on our own planet and elsewhere in the stellar universe, and with the use of laboratory experiments.

The rise of life on earth must be regarded as a process of successive complication of carbon compounds and the formation of multimolecular systems therefrom. On a formal basis one may divide this lengthy evolutionary process into a number of stages or steps:

1. The appearance of hydrocarbons and their closest derivatives during the formation of the earth as a planet and during the formation of the earth's crust, the atmosphere and the hydrosphere;
2. The conversion of the initial hydrocarbon compounds on the earth's surface into increasingly complex organic substances. The rise of the so-called "primordial broth";
3. The "self-formation", within this "broth" of individual open systems capable of interacting with the surrounding milieu, and, on this basis, of growing and reproducing (the formation of so-called protobionts); and
4. The further evolution of the "protobionts", the perfection of their metabolism, molecular and supermolecular structure on the basis of prebiological selection; and the rise of primeval organisms.

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It is immediately evident from what has been said how complex is the problem of the origin of life, and how extensive is the scientific research required for its solution—research flanked on the one side by cosmogenic and astronomical studies, and on the other by comparative-biochemical and physiological investigation of a variety of existing organisms.

The initial stage of the evolution of life, which is the abiogenetic formation of the very simplest organic substances (the hydrocarbons and their closest derivatives) is very widely encountered in the universe (Merrill, 1963). It is taking place at this very moment on the most varied objects in outer space. This stage of evolution is therefore accessible to direct study to a definite degree, and our knowledge in this area will increase in proportion as man penetrates outer space.

The compounds of carbon and hydrogen, particularly methane and the hydrocarbon radicals, may be observed both on the surface of stars (our own sun, in particular) (Kluber, 1931), where there are temperatures of several thousand degrees and very powerful gravitation, and within interstellar space, where one finds extremely weak gravitation and temperatures close to absolute zero (Kramers and Haor, 1946).

In this connection, not only the study of interstellar matter itself, but also the investigation of comets (Whipple, 1961), are matters of interest. These bodies, which are formed under conditions approximating those of the interstellar medium, contain an abundance of light hydrocarbons and cyanogen, as is readily observed when they penetrate the interior of the solar system. Enormous amounts of methane are found within the solar system itself—in the atmospheres of the large planets (Adel, Seipher, 1932; Kuiper, 1952) and in those of their satellites (Kuiper, 1944).

Particular attention just now is being directed to hydrocarbon compounds within meteorites (Vinogradov, 1965), first of all because meteorites are the only nonterrestrial objects which we can study directly, either chemically or mineralogically, and secondly because there is a similarity between meteoritic material and the material from which our own planet was formed.

The so-called carbonaceous chondrites are a class of meteorites which contain a significant quantity of carbon. The carbon occurs sometimes in pure form, but principally in hydrocarbons and hydrocarbon derivatives which contain oxygen, nitrogen or sulfur. These compounds are sometimes very complex and high-molecular (Vdovykin, 1962); some of them are quite similar to the organic substances found in terrestrial organisms (Vallentyne, 1965)—a fact which gave rise to the speculation that either meteorites or their parent bodies (asteroids) at one time contained living matter, and that the organic substances contained in the carbonaceous chondrites are the products of the secondary decay of extraterrestrial organisms (Nagy, Menschein, Hennessy, 1961). /658

At the present time, however, this opinion must be discarded completely, on the basis of a series of data which indicate that meteoritic organic material arose abiogenetically (Anders, 1961, 1964). Some present-day writers (J. Bernal in particular) suggest that the organic substances out of which our terrestrial organisms were created were themselves formed not only before the rise of life but even before the formation of the earth as a planet.

These substances, in the opinion of Bernal (Briggs, 1962; Bernal, 1965) made their appearance on earth in finished form as a part of planetesimals (planetesimals, from which planets of terrestrial type were formed, are comparatively small, cold accumulations of interstellar dust, similar in chemical composition to meteorites).

According to this hypothesis, our planet must have received its initial stock of carbon compounds during the very process of planetary formation. Following this, the earth gradually "fattened" itself on organic substances arriving out of space in meteorites and comet material—just as it continues to do today. However, the amount of organic material obtained in this way was comparatively small (Miller and Urey, 1964); we must assume that the basic mass of organic material necessary for the appearance of life had already appeared on the planetary surface at the time of the formation of the earth's crust.

One very indicative fact is that we can observe the abiogenetic formation of hydrocarbons taking place at a number of points on the earth's surface, as a result of the still uncompleted formation of the crust (Robinson, 1964).

Of significant interest in this respect are the releases of gas which were observed recently in the Khibinskiy Massiv on the Kola Peninsula (Petersil'ye, 1962). Analysis of these gases has revealed the presence of methane and also some heavier hydrocarbons. A very thorough examination of the physico-chemical and geological conditions of this region definitely indicates the abiogenetic origin of these gases.

Thus, all data obtainable through the study of contemporary space and geological phenomena constitute convincing evidence that during the formation of our planet and in the initial periods of its existence, significant amounts of hydrocarbons and hydrocarbon derivatives were formed on the earth's surface, and that it was these substances which formed the basis for the subsequent evolution of organic matter.

How can we trace the course of this evolution? Although direct geochemical observations of the transformation of organic substances under present-day natural conditions outside of living organisms are of some interest in this connection, the results of such observations cannot be used directly in judging the course of the abiogenetic evolution of organic substances on the surface of a still lifeless earth (during the so-called pre-actualistic period of its development), since the conditions existing at one time in the primeval terrestrial atmosphere and hydrosphere have been essentially altered (Rutten, 1962).

These initial conditions can be described basically as follows:

1. The absence of free oxygen in the preactualistic atmosphere, as a result of which there was no possibility of direct, penetrating oxidation of reduced hydrocarbon compounds;
2. An abundance of short-wave ultraviolet radiation, which penetrated the entire atmosphere and reached the surface of the earth. This created much greater opportunities for abiogenetic photochemical processes than are present in connection with the long-wave radiation which reaches the earth's surface in our own era; and
3. The absence of living organisms, whose metabolism as we know it today readily exercises an influence on a variety of organic compounds.

At the present time no such conditions exist naturally anywhere on earth. The ozone screen which exists at a height of 30 kilometers above the earth prevents any short-wave ultraviolet radiation from reaching the ground. The present-day atmosphere, the upper portion of the soil, and the hydrosphere down to great depths, are rich in free oxygen; they also support a dense population of microbes which, absorbing the organic substances in their environment, prevent any possibility of lengthy evolution of the latter, as Charles Darwin (Darwin, 1887) pointed out in one of his writings.

No matter how paradoxical it may seem at first glance, we must admit that the abiogenetic rise of life is no longer possible under natural conditions precisely because life already exists, and because there has been a sharp change in conditions which has precluded the possibility of any sort of prolonged evolution of organic substances along the routes followed by evolution during the preactualistic epoch of the earth's history.

We are therefore compelled to form a judgement of the earlier appearance of life on our planet mainly on the basis of laboratory experiments in which the physical and chemical conditions formerly existing on the earth's surface are artificially re-created. In so doing we proceed on the basis of the universally accepted tenet that the chemical potentials of methane, or any other organic substance, are invariable; in other words, they are the same as they always were, whether in the primeval terrestrial atmosphere, or in its successor, or in the test tube of a modern chemist. Therefore, in deliberately re-creating the conditions of the preactualistic epoch, we are justified in expecting results which will enable us to judge events which occurred in the remote past.

The extensive body of data existing at the present time demonstrates the extraordinarily high degree of reactivity of the hydrocarbons and their derivatives.

In the early era, external sources of energy must have played a very important role in organochemical reactions—primarily short-wave ultraviolet light, local increases in temperature, radioactive emanations, and, finally, sparks and quiet discharges in the atmosphere.

Employing these same sources of energy under laboratory conditions simulating those of the primeval surface of the earth has made it possible, in a number of experiments, to synthesize a very large number of biologically important substances. The raw material chosen for these syntheses consisted of such primitive compounds of the reducing atmosphere as methane, ammonia and water vapor, and some derivatives easily formed from them (for example, cyanogen, formaldehyde and acetylene). Many of these studies were reported at the Moscow Symposium on the Origin of Life on Earth, held in 1957 (Oparin, 1959), at the conference on the rise of prebiological systems held in Florida in 1963 (Fox, 1965), and, finally, at the colloquium on biogenesis held in Paris in 1965 (Gavaudon, 1967).

The majority of studies of this sort have been devoted to the synthesis of amino acids and nucleotides—which, upon being polymerized, make possible the synthesis of proteins and nucleic acids (Miller, 1959; Abelson, 1957; Pavlovskaja, Pasyanski, 1959; Harada, Fox, 1965; J. Oro, 1963; etc.)

Recent laboratory experiments conducted by a number of writers—/660
S. Akabori (Akabori, 1955); S. Fox (Fox, Harada, Vegotsky, 1959); K. Grossenbacher (Grossenbacher, Knight, 1965); G. Schramm (Schramm, Pollmann, 1962); and S. Ponnamperna (Ponnamperna, Sagan, Mariner, 1963); among others—have demonstrated quite convincingly that under the conditions present on the surface of the preactualistic earth amino acids and mononucleotides must have been polymerized, being joined in long molecular chains—which would lend to the formation of high-molecular substances like proteins and nucleotides, those very important components of protoplasm. However, the proteins and nucleic acids obtained from the protoplasm of present-day organisms possess a very definite molecular structure which is strictly determined by the position of the amino acids or mononucleotides in the polymer chain, and by the twisting of the chain (its position in space). By contrast, the structure of the abiogenetic amino-acid or nucleotide polymers must have been of random character, as can be demonstrated experimentally in the laboratory.

Thus at the present time we have made convincing observations and collected numerous experimental data supporting the conclusion that during some definite period of the preactualistic epoch of our planet, the basins of the hydrosphere, in addition to aqueous solutions of inorganic salts, also contained a variety of organic substances—simple and complex polymers and monomers, as well as energy-rich compounds capable of entering into numerous interactions. This peculiar "primordial broth" was continually changing and evolving.

However, the character of the chemical transformations of organic

substances, and the formation and decay of the latter, were radically different from those which are characteristic of living organisms. In the case of living organisms the succession of reactions is strictly consistent within a single metabolic network, thanks to the pre-existing organization of such organisms. For this reason, processes carried out within living organisms are quite "purposeful", and capable of securing the constant repetition of the synthesis of sometimes quite complex and specific compounds, which may arise and be stored within the cell in significant quantities (Oparin, 1965, 1964).

In the "primordial broth" there was, of course, absolutely no such "law and order". Within the simple aqueous solution of organic substances formed in the "broth", chemical transformations proceeded only according to the general laws of physics and chemistry. They were without a directed, organized character; they proceeded at random, along every physically possible route.

The task of the investigator working on the problem of the origin of life consists first of all in determining the evolutionary means by which out of a chaos of confused and conflicting reactions, there arose that definite metabolic order which underlies the life process itself. Life does not consist of the substances of the "primordial broth" scattered about in space; rather it consists of organisms—discrete systems which are spatially distinct from their environment, though interacting with it in the manner of closed systems.

The stability of this sort of system, and its longevity, are by no means invariable quantities: they are determined by recuperation, by the constant transformation of substances, by a regular combination of synthesis and decay which together comprise what we call biological metabolism.

A characteristic feature of living systems is that the whole network of metabolic reactions is not only strictly coordinated, but is purposefully directed toward constant self-preservation and self-renewal of the entire system under given conditions of the environment (Oparin, 1964). Such highly organized purposefulness, characteristic of living organisms, could not have arisen by accident. It could develop only during a process of gradual perfection, the motive power of which must have been a phenomenon similar to natural selection, since it is only on such a basis that we observe the "purposeful" improvement of organization in present-day living organisms.

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In view of these considerations, those very simple systems which were the prelude of life must have been formed spontaneously in the "primordial broth"; from the moment of their formation they must have been closed systems (Prigogine, 1955) interacting with the environment—systems capable of serving as an object for prebiological natural selection. The whole astonishing perfection of intracellular organization which we see in living organisms, the whole "purposefulness" of that organization, could have arisen only in the process of such selection.

What were they like--those formations which appeared spontaneously in the "primordial broth" as the first stage of evolution?

Two different answers to this question are found in the scientific literature.

Many present-day writers regard as the prime property of living matter the ability of organisms to effect precise self-renewal based on the replication of nucleic acids. They believe that those systems spontaneously formed in the "primordial broth" as the precursors of subsequent living things consisted of individual molecules of the nucleic acids (Muller, 1955).

Obviously, the ability referred to is an important factor in defining what we mean by the term life; it is one of the most characteristic features of living things as we know them: but one cannot conclude from this that it was necessarily a primeval or primary characteristic. The ability of self-renewal would appear rather to have been the culmination of those very ancient processes which led to the rise of organisms of modern type. A different point of view, therefore, is legitimate--we can suggest that the first step consisted of primitive metabolism unassociated with enzymatic action, but leading to the synthesis of nonspecific polymers and the multimolecular systems formed therefrom, the self-renewal ability of which stands at a very low level and does not depend upon the precise replication of nucleic acids, which appeared only during the evolution of these systems (Commouer, 1965).

Let us try to visualize experimental means for verifying these two points of view.

According to the first point of view, various polynucleotides arose in the "primordial broth", specifically an individual molecule resembling the RNA of the tobacco virus (Haldane, 1965). This molecule was without "purposeful" structure; the sequence of the monomers in its chain may have been random, or even entirely monotonic. However, on the basis of complementation, such a molecule would be able to replicate, to "reproduce" in the "primordial broth". As a consequence of the great imperfection of this replication in vitro there would arise large numbers of mutations, and also great diversity in the nucleic acid molecules owing to varying positions of the radicals. On this basis there would be selection of the most rapidly synthesizing and multiplying molecules, the result being the rise of RNA and DNA in their present-day forms.

However, any experimental re-creation of this phenomenon based on models would contribute nothing more than a unique collection of homologous molecules resembling layers of ozocerite. There cannot be any sort of natural selection at such a molecular level, since for a particular polynucleide chain to acquire an advantage in growth rate, there must first be code relations between the polynucleide and a protein capable of serving as a specific catalyst for the more rapid "reproduction" of precisely this molecule.

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As A. Rich (Rich, 1962) points out, this is precisely where the hypothesis encounters its greatest difficulties, "since in order to achieve the development of biochemical systems of information transmission, it is first necessary that the sequence of nucleotides be correlated with the sequence of amino acids in the protein. We must assume that the amino acid sequence has a definite specificity sufficient to assure execution of the catalytic functions necessary for the operation of the described system. In a word, we must try to discover means for the rise of activating enzymes." But for the conditions of a simple solution—the "primordial broth"—this is very difficult even on the theoretical level, and all the more in an experimental approach.

In our laboratory at the Institute of Biochemistry imeni A. N. Bakh, USSR Academy of Sciences (Oparin, Serebrovskaya, Vasil'yeva, Balayevskaya, 1964), we mixed solutions of various polypeptides and polynucleotides, and both natural proteins and nucleic acids, and artificially synthesized compounds (polyadenine and polylysine, for instance). Given ordinary temperatures and acidity, even very dilute solutions supplied individual multimolecular formations (coacervate drops, Fig. 1) visible under the microscope. In these there occurred a joining of polymer molecules, which almost entirely disappeared from the surrounding solution, whereas the polymer concentration in the drops reached 50 percent and more.

An analogous phenomenon was observed when we polymerized the nucleotides in the presence of a polypeptide or during the formation of a polypeptide (for example, polylysine) (Fig. 2).

Once the number of polymer molecules reached a certain figure, the homogeneity of the solution was disrupted and coacervate drops appeared.

The arrangement of monomers in the polymer chain did not play any perceptible role; the appearance of drops depended only on the degree of polymerization.

These experiments demonstrated that under conditions of the "primordial broth" there was simultaneous formation of polypeptides and polynucleotides, which must have been joined in multimolecular systems (coacervate drops), and that subsequent evolution took place in these systems, and not merely in the solution, on the molecular level.

The formation of coacervates from nonspecific polymers can be taken as the simplest illustration of the principle on which the formation of biological supermolecular structures is based.

For example, protein-lipid membranes—very typical structures of any living cell—do not require strictly determined specific proteins and lipoids for their production. All that is necessary is a combination of the indicated substances for compounding relations between the hydrophilic and the

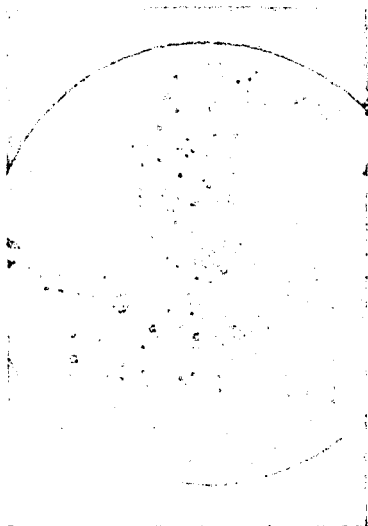


Figure 1. Coacervate Drops from Polyadenylic Acid and Polylysine.



Figure 2. Coacervate Drops formed during Synthesis of Poly-A in the Presence of Histone.

hydrophobic sections, and distribution of charges, etc. (Gel'man et al., 1966).

There is an extensive body of comparative-biological data which indicates that no rigidly specific chemical composition of components was required for the formation of the primordial multimolecular structures and systems. This situation remains evident among present-day bacteria; standardization of the composition appeared only at a very high stage of evolution.

On the basis of these considerations, it is inescapable that, at a certain stage of evolution of the "primordial broth", there occurred the formation of numerous and quite varied multimolecular structures and complexes within it, and that these were separated from the general solution in the form of isolated systems. These structures may have been similar to Goldacke's "vesicles" (Goldacke, 1958), or Fox's microspheres (Fox, Fukushima, 1964), or our own coacervates, and numerous other formations of this sort. In order to evolve, however, these structures had to interact with the surrounding solution in the manner of closed systems, so that their stability was not static, but dynamic and "steady-state" in character. From this point of view coacervate drops can be regarded as the most convenient, but certainly not the only possible, models for simulating the phenomena of the remote past which we are discussing.

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Coacervate drops form readily even in very dilute solutions of various nonspecific polymers (polypeptides, polynucleotides, polysaccharides, lipoids, etc.) They stand out as individual systems isolated from the environment by distinct boundaries; however, they are capable of selective adsorption of various substances, such as dyes, amino acids, sugar, and the like.

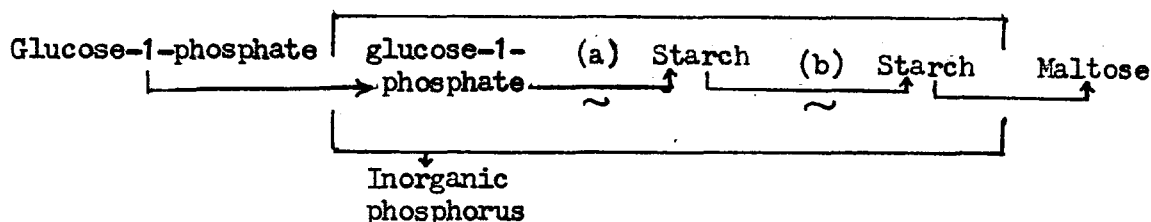
The concentration of the indicated compounds is sometimes tens and even hundreds of times greater than in the surrounding medium. If the substances thus adsorbed exert a catalytic action, then chemical reactions arise in the drops which convert them into open systems (Yereinova, 1962).

For modeling the phenomenon in question we usually employed ferments as catalysts, with due allowance for the fact that the "primordial broth" contained no ferments.

At the given stage of research, the use of such powerful and specific catalysts offered us an enormous advantage in time. It is understood, of course, that the experiments could have been conducted with the use of more primitive catalysts.

Introducing various ferments into the coacervate drops, we were able to induce in the latter an acceleration of a number of the reactions—oxidation-reduction, phosphorylation, polymerization, etc. (in other words, the transformations which, according to the data of comparative biochemistry, underlay the primary processes of metabolism common to all organisms, including present-day ones).

By way of example I include here a diagram illustrating one of our experiments (Oparin, Yevreinova, Larionova and Davydova, 1962). The rectangle denotes a coacervate drop formed from histone and polyglycoside:



The ferments glucosyltransferase (a) and β -amylase (b) were introduced into the drop. In the surrounding medium were glucose-1-phosphate, entering the drop by diffusion and being converted there into starch, which broke down under the action of the β -amylase into maltose which was released into the surrounding medium, where it had not been before. Thus a continuous flow of substances through the drop was created—an elementary simulation of metabolism. In this situation the drop maintained itself as an open system for an extended period; the transformations within the drop proceeded as long as the reaction rates (a) and (b) were in equilibrium.

However, if reaction rate (a) significantly exceeds reaction rate (b), or if the second reaction is absent, then the drop, in addition to maintaining itself, will actually increase in size and weight—it will grow at the expense of the newly synthesized polymer. This can be seen from the curve

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of growth measurements. It can be seen from the graph that the volume of such a drop nearly doubled in the course of the first 30 minutes (Fig. 3).

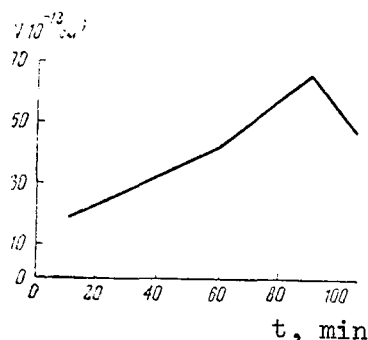


Figure 3

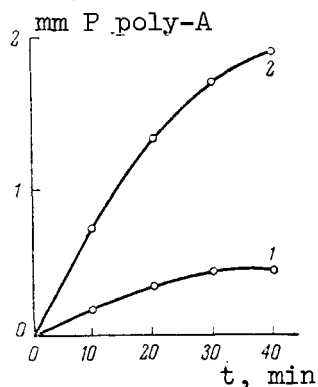
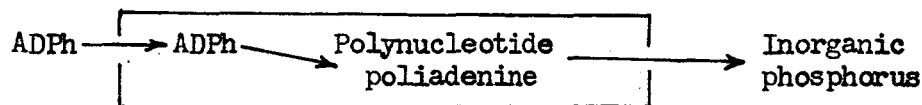


Figure 4

Figure 3. Increase in the volume of a coacervate drop during synthesis of starch within it.

Figure 4. Synthesis of poly-A polynucleotidephosphorylase in coacervate drops in the presence of hexokinase.
1 - polynucleotidephosphorylase; 2 - polynucleotidephosphorylase + hexokinase.

Analogous means can be used to induce the enzymatic decay or synthesis of polynucleotides entering into the composition of coacervate drops, as shown by the accompanying sketch (Oparin, Serebrovskaya, Auerman, 1961). To secure such synthesis in coacervate drops formed from RNA histone, we inserted bacterial polynucleotidephosphorylase, dissolving adenosine diphosphate (ADPh) in the surrounding medium as a substrate.



Open multimolecular systems similar to our models, capable of assuring primitive metabolism, might well have arisen in the "primordial broth". Of course the processes within such systems were accelerated only by very undeveloped organic and inorganic catalysts entering from the environment.

Increasing in volume and weight, such systems (for brevity we shall henceforth refer to them as protobionts) in the "primordial broth" must have first grown and then fractionated under the influence of external mechanical factors—for instance the action of surf or waves—just as the drops of an emulsion will do upon being shaken.

Protobionts, growing and subdividing, must have maintained a certain

constant interaction with the environment. In the synthesis of new polymeric molecules, the constancy of the composition of the growing protobionts would have been favored by the replication (based on compounding) of polynucleotides in the drops; the main factor, however, was that the protobionts maintained a constant ratio between reaction rates, as well as conformity in the nature of the reactions taking place within themselves. This was because the protobionts preserved within themselves, during growth, an increased concentration of the very simplest inorganic or organic catalysts, selectively absorbing them from the external medium.

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Of course, this hypothetical phenomenon, as far as constancy and precision are concerned, was in no way comparable to that observed in even the most primitive of organisms existing today. During growth and fractionation of the protobionts, any sort of deviation or shift might occur, especially if a change occurred in the environment. All of these factors working in conjunction must have led to the rise of a special sort of pregeological "natural selection" which trained the future evolution of protobionts along the path leading to the formation of primeval living organisms.

We were even able to secure a reasonable demonstration of this "selection", using our models with coacervates. We inserted a complex of catalysts in some of the drops, thus securing, under appropriate conditions, a comparatively rapid synthesis of polymers and growth of the system as a whole. In the case of other drops we used a less complete set of catalysts. Direct tests will show that the rapid growth of the first sort of drop at first depresses, and then completely eliminates, the growth of the second sort (Oparin, 1965) (Fig. 4).

Comparative-biochemical study of metabolism among the most primitive present-day organisms enabled us to suggest the sequential stages of the evolution of metabolism during progress toward living matter.

First of all, we had to deal with the catalytic apparatus involved in those stages, as the main factor in the organization of metabolism based on the ratio of the rates of its component reactions (Oparin, 1965). Of course, at the stage of evolution we were analyzing, the protobionts were restricted to the use of catalysts existing in the "primordial broth"—the very simplest organic substances and inorganic compounds, whose catalytic activity was very low. However, in appropriate combinations, this activity may have been raised considerably, as must have happened during the course of "natural selection" of the protobionts, the result being the formation of relatively primitive (for the modern living cell) catalyzers—the "coferments".

Many of these "coferments", or components thereof, are borrowed by present-day organisms in the form of vitamins from the environment, just as the ancient protobionts did.

The first protein-like polymers, with their random disposition of amino

acid radicals, may have served as material for the formation of coacervate drops and protobionts; they were, however, devoid of catalytic activity, or possessed it only in low degree.

In present-day organisms the synthesis of ferment proteins is effected through an extraordinarily complex and perfected mechanism, by which amino acids are successively "strung" on a polypeptide chain in an order required by the specific, rigidly regular combination of mononucleide radicals in DNA and RNA molecules. Of course, such a mechanism could arise only in the process of the lengthy evolution of living systems. But even at much earlier stages of development, polynucleotides introduced into protobionts must have exerted a definite influence on the polymerization of amino acids taking place in those systems.

The intramolecular structure of the most ancient polynucleotides was still very imperfect. During the process of growth of the protobionts, this structure would vary strongly. Any variation appearing in this way could, to a certain extent, entrench itself in the developing protobiont, as a result of compounding capability, and thus be able to exert an influence on the disposition of amino acid radicals being synthesized in the protobiont.

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If indeed the combinations of amino acid radicals formed in this way were favorable for intensifying the catalytic capability of the polypeptides, then the system generating such a combination would enjoy an advantage of more rapid growth and reproduction. In the opposite case it would be eliminated through natural selection. Thus, gradually the structure of protein-like polypeptides, together with that of their component polynucleotides, became more orderly, more adapted to those functions which the polymers served in growing and reproducing biological systems.

Under natural conditions, many hundreds of millions of years were required to establish the bases of biological metabolism and cellular structure—possibly a half of the whole period of time during which life has existed on earth. If we picture clearly the immensity of this evolution, how foolishly naive appear those quite recent attempts to re-create a sudden self-generation of life in rotting broths and infusions of organic substances. Having recognized the paths by which living substances came into being during the process of the evolution of terrestrial matter, we shall be in a position to re-create them artificially, not through the tortuous, slow means which nature employed, but within a relatively short time, by consciously selecting in our laboratories the necessary conditions and the necessary sequence of phenomena, replacing natural selection with a directed combination of substances, systems and processes. This path will lead us safely to the realization of a cherished dream of mankind—the artificial synthesis of living matter.

The success already achieved by using this approach enables us to speculate not only about this type of synthesis, but also about the long-range future of our problem.

CONCLUSIONS

The rise of life on earth was an "expected" event in the process of evolution of carbonaceous compounds and the multimolecular systems built up from them.

At the present time we have discovered objective methods for the study of this process, both through observing phenomena in the world around us, and through laboratory experiments which simulate the events of the remote past.

Research which has widely developed on this basis, and the results already obtained, reveal to us in rough outline the course of the evolution of matter which led to the appearance of life.

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